REMARKS

Claims 11, 14, 15, 17, 19, and 20 currently appear in this application. The Office Action of July 30, 2002, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

Claim Objections

Claim 14 is objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 11 has been amended to delete "26-homo-1 α,25-dihydroxy vitamin D_3 22-oxacalcitol" in favor of --26-homo-1 α,25-dihydroxy vitamin D_3; 22-oxacalcitol-- .

Rejections under 35 U.S.C. 112

Claims 17, 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

This rejection is respectfully traversed. Claims 17, 19 and 20 have been rewritten to clarify the invention claimed therein. These amendments are supported in the specification as filed at page 3, line 26 through page 4, line 5 and page 6, lines 11-19.

Art Rejections

Claims 11, 14, 15, 17, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dam et al. in view of Itoh et al., Hingorani et al., and Muller et al. Dam et al. are said to teach that calcitriol and calcipotriol are useful in suppressing the number of Langerhans cells when applied topically. Dam et al. are also said to teach that calcitriol or calcipotriol inhibit THF-α, a factor which can induce migration of Langerhans cells. Dam et al. are also said to teach that calcitriol and calcipotriol suppress the T-cell proliferation. The Examiner concedes that Dam et al. do not teach calcitriol in the form of an ophthalmic solution, nor teach that calcitriol is useful in treating keratoconjunctivitis and preventing phlyctenular keratitis or corneal infiltration. The Examiner also admits that Dam et al. do not expressly teach that calcitriol is useful in a method for inhibiting interleukin-1 production in cornea epithelium. Itoh et al. are said to teach that calcitriol can be formulated

into an ophthalmic composition. Hingorani et al. are said to teach that atopic keratoconjunctivitis is a T-cell inflammation prominent disorder, as well as that atopic keratoconjunctivitis may lead to infiltration and corneal involvement such as epithelial keratitis. Muller et al. are said to teach that calcitriol inhibits the production of interleukin-1 at a presecretory level such as reducing the levels of interleukin-1 α mRNA.

This rejection is respectfully traversed. Claim 11 has been amended to recite a method for inhibiting Langerhans cell migration wherein the inhibition of Langerhans cell migration results in the prevention or treatment of keratoconjunctivitis, phlyctenular keratitis, or corneal infiltration. There is no teaching or suggestion of this phenomenon in the cited references.

Dam et al. merely teach that calcitriol decreases the number of Langerhans cells on human skin. There is no way that one skilled in the art would be led to believe that the specific vitamin D compounds of claim 11 would inhibit the migration of Langerhans cells in the eye. Furthermore, prior to the present invention, it had not been known in the art that a vitamin D compound is useful in preventing or treating the ocular disease keratoconjunctivitis, phlyctenular keratitis, and corneal

infiltration, wherein an ocular inflammation site extends to the cornea.

It should be noted that the inhibitory effect of the vitamin D compounds on Langerhans cell migration and the effectiveness of the claimed compounds in preventing or treating an inflammation of the cornea via this inhibitory effect have been discovered by the present inventors. It should also be noted that the compounds can treat such an inflammation **without** lowering the transparency of the cornea, as described in the specification as filed at page 6, lines 17-19. There is nothing in the cited art that would predict this effect.

In other words, the present inventors have discovered a new use for the compounds recited in claim 11, namely, that these compounds inhibit Langerhans cell migration and that these compounds are effective in preventing or treating an inflammation of the cornea via this inhibitory effect. Importantly, the present inventors discovered that these compounds prevent or treat corneal inflammation without lowering the transparency of the cornea. This effect could not have been predicted from the cited prior art.

In view of the above, it is respectfully submitted that the claims are now in condition for

allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,
BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By _____
Anne M. Kornbau
Registration No. 25,884

Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
AMK:nmp
G:\BN\Y\YUAS\KINOSHITA3\Pto\oct 29 02 amend after final.doc

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11. (Third Amendment) A method for ~~inhibitory~~ **inhibiting** ocular Langerhans cell migration in a mammal comprising administering an effective amount of a Langerhans cell migration inhibitor comprising a compound selected from calcitriol; 1α,24-dihydroxy vitamin D_3; α-calcidol; calcifedol; 1α, 25,26-trihydroxy vitamin D_3; 1β,25-dihydroxy vitamin D_3; 24-homo-1α,25-dihydroxy vitamin D_3; 26-homo-1α,25-dihydroxy vitamin D_3; 22-oxacalcitol; and calcipotriol as an active ingredient to the mammal**, wherein the inhibition of said ocular Langerhans cell migration results in the prevention or treatment of keratoconjunctivitis, phlyctenular keratitis, or corneal infiltration**.

17. (Twice Amended) The method of Claim 15 wherein the **inhibition of the** Langerhans cell migration ~~causes~~ **results in the prevention of treatment of** keratoconjunctivitis.

19. (Twice Amended) The method of Claim 15 wherein the **inhibition of the** Langerhans cell migration ~~causes~~ **results in** phlyctenular keratitis or corneal infiltration.

20. (Twice Amended) The method of Claim 15 wherein the inhibitor prevents and/or treats an ocular inflammation **wherein the inhibition of the Langerhans cell migration results in the prevention or treatment of an ocular inflammation** by inhibiting the production of interleukin-1 in corneal epithelial cells ~~**caused by Langerhans cell migration**~~.